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DIPHTHERIA INFECTIONS, WITH PARTICULAR REFERENCE TO CARRIERS AND TO WOUND INFECTIONS WITH B. DIPHTHERIAE

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Seventy-five cases of diphtheria and 102 diphtheria carriers were treated at the Walter Reed General Hospital during the period from Oct., 1918, to Aug., 1919. Thirty-seven of the infections developed in persons who were living in the hospital either as enlisted attendants or as patients admitted for other conditions.

Theoretically it should be possible to stop the spread of diphtheria in institutions, either by the isolation of all cases and carriers; or by the immunization of all nonimmune persons. The former method, which is the one generally used, in both civil and military hospitals, was carried out with rather poor results. Immediately following the bacteriologic diagnosis of a diphtheria case, or carrier, the patient was transferred to the proper isolation ward. Throat cultures and Schick tests were made of all men who had been in contact with him, and when indicated, these contacts were immunized with diphtheria toxin-antitoxin mixture. All cultures were saved and an effort was made to determine the virulence for guinea-pigs and the special cultural characteristics of each.

A direct relationship apparently existed in a number of instances, between carriers and clinical cases. Twelve cases and 14 carriers were found to have been in contact with A——, a nasal carrier, who had been a waiter in the main mess hall. This man gave no history of diphtheria but had suffered with a chronic rhinitis for five years. Cultures of both nares continued to yield diphtheria bacilli mixed with pyocyaneus in spite of treatment, for months. The importance of this case is doubtful as the diphtheria bacilli isolated were avirulent for guinea-pigs. However, as little is known concerning the possible changes in virulence following the transfer of organisms from one

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human being to another, it is mentioned. In one small group of surgical patients who habitually played cards together, three cases developed and four carriers were found. On Feb. 15 four carriers were found among the members of a band that had been transferred as a unit from Camp Greenleaf. Diphtheria bacilli were also obtained from the mouthpieces of musical instruments used by these men. M——, who carried virulent bacilli, was treated for 8 weeks and returned to duty after the required number of negative cultures. Two weeks later another musician, who slept in the bed next to his, developed a severe case of laryngeal diphtheria. Cultures made at this time of both men contained the same type of virulent diphtheria bacilli as those originally obtained from M——.

GROUPING OF CASES

The cases considered here have been divided into three groups as follows: (1) throat carriers; (2) wound carriers, and (3) active wound cases.

The first group has been subdivided into (a) convalescent carriers, or those who have had active diphtheria and who harbor diphtheria bacilli in their throats during convalescence; and (b) contact carriers, who, as the name implies, became carriers through contact with other carriers or active cases of diphtheria, without having the disease clinically.

The term wound carrier is applied to patients whose wounds contained diphtheria bacilli, but showed no signs of an active diphtheric process. Organisms were isolated from amputation stumps, thoracotomy wounds, shrapnel and other flesh wounds and bone sinuses. All of these wounds showed granulation tissue which was apparently healthy. The presence of the diphtheria bacilli did not seem to prevent or delay healing. Positive cultures were obtained in a number of instances up to the time when the wounds had completely healed.

Into group 3 have been placed all active wound cases showing a membrane with accompanying inflammatory changes. The membranes were usuaully whitish, gray or grayish-green in color, with raised, well defined edges. They were tightly adherent, and on being stripped left bleeding surfaces. In two cases the membranes extended over the edges of the wounds on to the surrounding skin. Pain and tenderness were marked symptoms in all of these cases. Wound carriers, on the other hand, rarely complained of tenderness and never of pain in their wounds. General reactions of the cases varied. In the severe ones the temperature remained around 102 and 103 F., while the pulse rate was from 100 to 120. In others, however, there was only a slight elevation of the temperature and pulse rates, and the patients complained only of painful wounds; in fact, some of them objected to staying in bed.

Routine cultures of the nose and the throat were made of all patients admitted to the isolation wards and three successive negative cultures, made at three-day intervals, were required before their release. When wounds were present cultures were made from them. The guinea-pig virulence of the organisms from each case was determined as soon as possible, and carriers of virulent organisms were separated from carriers of avirulent organisms. Schick tests were made on most of the patients, and all those showing a positive reaction were given three 1 c.c. injections of diphtheria toxin-antitoxin mixture at 7-day intervals.

TREATMENT

Patients with active cases of diphtheria, it need scarcely be said, were given antitoxin during the acute stage. When convalescent they received the same treatment as that given contact carriers, which consisted of local applications of various antiseptic solutions and in selected cases, surgical removal of infected foci. In the treatment of many of the cases Dobell's solution was used as a gargle, and as a nasal and pharyngeal spray, at 8 a. m. and 4 p. m. each day, with liquor antisepticus alkalinus in the same manner at noon and at 8 p. m. Cultures were made from the nose and throat of all carriers, after the second week in isolation; and from the crypts of the tonsils, after thoroughly scrubbing the tonsillar surface with antiseptics, such as dichloramine-T, phenol, 5%, in glycerol, or Dakin's solution. Those showing positive crypt and negative nasal cultures, were transferred for tonsillectomy. The treatment of the patient whose history is given in the following, who on admission had positive nasal, tonsillar and tonsillar crypt cultures, is of interest:

2/14.—Admitted to isolation ward. Dobell's gargle and spray every 4 hours; 10% silver nitrate swabbed on tonsils every other day. All cultures continued positive.
3/13.—Tonsillectomy.
3/14–3/28.—Dobell's gargle and spray every 4 hours.
3/28–5/ 1.—Argyrol, 10%, in nose and throat twice daily.
4/27–5/ 6–5/16.—Toxin-antitoxin mixture, 1 c c, subcutaneously.
5/ 1–6/27.—Dobell's solution gargle and spray with alkaline antiseptic solution as gargle and spray every 4 hours.

6/21–7/31.—Dichloramine T., 2%, in oil swabbed in throat, and used as nasal spray 3 times daily.
7/31–8/15.—Still in isolation with positive nasal cultures.

The number of wound carriers was so small and the treatment so varied that we do not feel justified in forming any definite conclusion as to the best method of handling them. The following applications were used: Dakin's solution, irrigations at intervals of 2 hours, argyrol crystals, tincture of iodine, alcohol and saturated alcoholic solution of gentian violet. All of these antiseptics were used at different times on some of the cases. Daily cultures were made of all patients before the morning dressing. The following is an outline of the treatment of three of these wounds:

R. D.:	5/15–5/20.	Argyrol crystals on wound once daily.
	5/20–6/16.	Tincture of iodine swabbed on wounds once daily.
	6/16–7/11.	Dichloramine-T, oil solution once daily.
	7/11.	Discharged as negative.
J. R.:	3/20–3/30.	Dakin's solution irrigations every 2 hours.
	3/30–4/30.	Dichloramine-T, once or twice daily.
	4/30–5/15.	Zinc oxide ointment once daily.
	5/15–6/22.	Wound healed. Cultures positive until closed.
H. N.:	4/ 9–4/19.	Dakin's solution irrigations every 2 hours.
	4/20–4/30.	Dichloramine-T twice daily.
	4/30–5/10.	Dakin's solution irrigations every 2 hours.
	5/22–6/19.	Tincture iodine once daily.
	6/19–6/28.	Dakin's solution twice daily.
	6/28–7/18.	Dichloramine-T twice daily.
	7/18–8/ 3.	Gentian violet, saturated alcoholic solution, applied to granulating surfaces injected into granulating tissue and under the edges of the epithelium.
	8/ 3.	Discharged from isolation with negative cultures.

Frequently when superficial cultures of these wounds became negative, the organisms could be readily obtained by curetting a small area and taking cultures from the tissues just below the surface. This fact was also noted by Simmons [1] in a series of thoracotomy wounds infected with diphtheria bacilli.

All cases of active wound diphtheria were treated with diphtheria antitoxin, given subcutaneously, intravenously or intramuscularly. The three following histories are illustrative:

R. W., aged 20, a white man, had measles, chickenpox, and whooping cough when small; pneumonia 1905. Tonsillectomy in 1908. No history of diphtheria. Gonorrhea in 1916.

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[1] Jour. Infect. Dis., 1919, 25, p. 219.

On Aug. 8, 1918, Vesle River, France, shrapnel wounds both thighs and cheek bones (right). Left femoral artery severed by shrapnel. Bleeding checked and wounds bandaged at relief station; same night removed to evacuation hospital and left leg amputated at lower third of thigh. Sept. 14, to Base; Nov. 23 to U. S., and to Staten Island Hospital, where 3 inches of bone were removed from stump on Dec. 7; to Walter Reed General Hospital Dec. 27.

Condition on Admission: Sitting up in wheel chair, general condition good. Granulating area about 2 inches in diameter at site of incision in amputation wound. Stump swollen and red. Acutely inflamed.

Special senses normal. Skin and mucous membranes normal. Glandular system: enlargement of left inguinal glands; otherwise normal. Vascular system normal. Heart and lungs normal. Abdomen showed no abnormality. Liver and spleen not felt. Nervous system normal. Amputation at mid third of left thigh with inflamed granulating area about 2 inches in diameter.

Feb. 8: Unimproved. Hot packs, Feb. 12, Bact. count 30 per field.

Feb. 15: High bacterial count. Bichloride packs. Cultures: Staph. aureus.

Feb. 21: Stump culture showed diphtheria bacilli. Throat culture also positive for B. diphtheriae; admitted to isolation ward. Stump not tender. No membrane. Temperature normal. Diagnosis: Diphtheria carrier, in throat and wound. Schick test negative.

March 6: Released from isolation, after three negative cultures. No improvement. Dichloramine-T dressings.

April 1 to April 8: Dichloramine-T dressings.

April 8 to April 12: Dakin's q.2.h.

April 12: Stump became tender and painful to touch. Diphtheria bacilli present in cultures. Membrane began to form.

April 15: Admitted to isolation ward. Tough, dirty, white membrane over end of stump. Tightly adherent. End of femur protruding. Membrane extends ¾ inch up inner side of the thigh. Stump and surrounding skin tender and painful to touch. Has had hot boric compresses to wound since April 12. Temp. 100. General malaise.

April 17: No change. Given 10,000 units antitoxin. No reaction. Temp. 100.2.

April 18: Edges of membranes are loose and shriveling. Feels better generally.

April 19: Membrane gradually loosening; stump less tender.

April 20 and 21: No change. All membrane loose except small patch near femur.

April 22: Antitoxin 10,000 units subcutaneously.

April 23: Membrane hanging by small piece. Temperature 100.

April 24: All membrane gone. Temperature normal.

April 25: Dakin's solution q.2.h.

May 5: Healing rapidly.

May 15: Three negative cultures.

July 23: Cultures negative for diphtheria bacilli. Sent to operating room for shortening of femur.

R. T., aged 22, a white man, had measles, mumps and whooping cough in childhood, and pneumonia in March, 1918. No wounds. Denied venereal infections.

Sept. 14, 1918, on shipboard on way to France had influenza and pneumonia. Empyema developed in right lower side of chest and rib was resected in anterior axillary line. Remained in Brest, and tube was left in 3 weeks; back to U. S., Jan., 1919. Arrived at Walter Reed Hospital April 28, 1919. On admission had no cough or pain. Wound was draining slightly. Weight was normal, 144 lbs. General condition good. Over right lower side of chest percussion was dull, B & V sounds were distant. Otherwise physical examination was not remarkable.

April 29: Scar 3 inches in right anterior axillary line; almost healed.

May 22: Transferred to empyema service. No further note found on empyema service until May 23.

May 23: Large open wound, apparently gangrenous; no discharge of any consequence. Two large drainage tubes and hot packs.

May 25: Staphylococcus and B. diphtheriae in wound. Transferred to isolation ward.

May 25: Patient transferred to diphtheria ward. Temperature and pulse subnormal. At site of thoracotomy incision was a wide gaping deep wound, the surfaces of which were covered by a grayish membrane, which extended down to the deepest visible part of the wound. Immediately around the edges of the wound, the skin had sloughed off, leaving a shining, red, raw surface. This extended about an inch from the edge of the wound. Immediately beyond this area began a thin reddish gray membrane extending over the skin for about 4 or 5 inches around the wound. Just beyond the membrane there was a zone of inflamed skin which was sharply demarcated from the normal skin. Disagreeable odor noticed. Patient seemed in a very poor condition. He vomited all fluids and food, had not retained anything by mouth for 2 days. Complained of blurring of vision; 10,000 units of antitoxin were given intramuscularly on the 24th and the same amount on the 25th.

May 27: More of the membrane on the skin had disappeared, leaving the shining red surface for about 4 inches around the wound. The wound itself was unchanged. No spread of the process on the skin. Temp. was 97 by rectum, pulse averages from 50 to 60. General condition unchanged. Had serum rash over body; 10,000 units antitoxin were given intramuscularly; 500 c c physiologic salt solution subcutaneously. Vomited everything taken by mouth. Blood cultures taken on the 26th showed no growth.

May 28: Much of the membrane on the skin had shriveled and much had disappeared. Wound unchanged. Typical fetid odor persisted. Extensive rash over whole body. Continued to vomit. Morning temp. 96; pulse 50; blood pressure 90/60; 1000 c c of 10% dextrose and levulose solution intravenously. Had not voided since morning of 26th. Bladder was not distended. Condition poor. Evening temp. 95.5; pulse rate 40; blood culture showed no growth.

May 29: Membrane on skin practically all gone, and redness had also disappeared. Wound unchanged; 500 c c normal saline solution subcutaneously; 700 c c of 25% dextrose and levulose solution intravenously at the rate of 200 c c per hour. He had hiccoughs since early morning. About 3:00 p. m., vomited 500 c c of dark brownish material. Microscopic showed few red blood cells and much debris. Severe nose bleed. Blood CO_2 37%. 6:20 p. m. began to spit up bright red blood, breathing became difficult, and he died at 6:30 p. m. Had not voided for 3 days; bladder not distended. Blood culture taken three days ago was still sterile.

Blood: May 28: Red blood cells, 4,448,000; white blood cells, 30,450; hemoglobin, 80%.

Differential Count: Polymorphonuclear neutrophils, 86%; small mononuclears, 8%; large mononuclears, 2%; transitionals, 4%.

Cultures of the throat for diphtheria bacilli were negative April 29, May 2, 4, and 28.

Cultures of the wound gave staphylococcus aureus and diphtheria bacilli May 25 and 27; cultures from all over the wound and surrounding skin May 28 gave diphtheria bacilli.

Necropsy: Thoracotomy wound with rib resection, right side; necrotic condition of edges; pleuritis organizing, right; petechial hemorrhages—skin, mesentery, omentum, stomach, intestines, epicardium, myocardium; pleuritis, chronic, left; lymphadenitis, bronchial, acute; carnification of lung right lower and middle; pneumonia, lobar, left lower; parenchymatous changes kidneys and liver.

Heart's blood: B. diphtheria; staphylococcus albus, streptococcus hemolyticus. Feces: B. diphtheriae. Lungs: B. diphtheriae; staphylococcus albus, streptococcus hemolyticus. Thoracotomy wound: B. diphtheriae.

M. L., aged 24, a white man, on Sept. 26, 1918, at the Verdun front, received a wound on the left buttock, from a high explosive shell; first aid in 6 hours; to Base hospital on 28th. Dressed daily until Nov. 15, when dislocated hip was reduced. Nov. 16, operated, incision and drainage. Dec. 1, incision and drainage of septic left knee. Dec. 20, incision and drainage of left thigh. Jan. 7, amputation of left thigh, at hip because of infection. Jan. 9, incision and drainage of abscess of left shoulder. Jan. 11, laryngeal diphtheria; received many injections of antitoxin. Feb. 15, pneumonia. Feb. 22, right side of chest aspirated. Sailed for U. S. March 8, and reached Walter Reed General Hospital April 11, 1919.

Condition on Admission: Unhealed disarticulation left thigh; undernourished; normal weight, 150 lbs.; present weight, 100 lbs. Teeth in bad condition. Gums: marked pyorrhea. Scar inner side left elbow. Entire right side of chest dull. Flat at base. Paresthesia fifth finger left hand. Large irregular scars left buttocks. Disarticulation of left thigh at hip. Three sinuses leading into hip. Marked general emaciation.

Progress: Wound treated and sinuses irrigated. Dakin's solution used.

May 5: Thoracentesis. No fluid. Roentgen ray showed increased density over lower right side of chest, less marked over upper part.

May 11: Thoracentesis; negative result.

June 9: General condition improved; less discharge from wound.

June 20: Thoracotomy. Incision and drainage C. D. dressing. Diagnostic puncture; nothing found. Culture taken this date showed gram-positive bacilli of the diphtheria group in thigh wound.

June 26: Admitted to isolation ward; B. diphtheriae positive.

June 27: Patient vomited all fluids and food given by mouth; pulse 120; temp. 97. The skin was dry and he seemed much in need of fluid. Wound showed an extensive thick diphtheritic membrane over most of the granulating surface. There was marked swelling and the wound was extremely painful. Over the skin surrounding the wound was a thin filmy grayish membrane, and just beyond the membrane was an area of erythema which was sharply demarcated and about 4 cm. beyond the edge of the membrane. Odor was fetid. Given 40,000 units of diphtheria antitoxin intravenously in the morning and 50,000 units intravenously in the afternoon; 500 c c normal salt solution intravenously; also proctoclysis.

June 28: Condition improved; pulse better volume; temp. 99 during night; 250 c c dextrose and levulose solution 25% intravenously at rate of 200 c c per hour. Hot boric dressing to wound. No change noted. Given 50,000 units antitoxin intravenously.

June 29: Continued to vomit. Large piece of membrane loosened and erythematous area of skin less. One liter 25% dextrose and levulose solution intravenously.

June 30: General condition about the same. Membrane about the same. Continued proctoclysis; 50,000 units of antitoxin in 600 c c normal salt solution intravenously.

July 1: Unable to retain anything by mouth. Edges of the membrane looser and a piece had sloughed off. Given 80,000 units of antitoxin in normal salt solution; 200 c c 25% dextrose and levulose solution intravenously. Pulse steadily weaker. Died 11:30 p. m. No urine voided during last 3 days of life. Bladder was not at any time distended.

Throat Cultures: April 11, B. diph. and Strep. hemolyticus absent. June 29, B. diph. absent.

Nasal Cultures: June 29, positive in both sides for B. diph.

Stump Cultures: June 20: Gram-positive bacillus of diphtheria group. June 25: B. diphtheriae. June 27: B. diphtheriae in skin and membrane on skin surrounding wound. June 29: All areas of wound positive for B. diphtheriae.

Necropsy: Abscess, post pleural, right; bronchopneumonia, right. Diphtheric infection, amputation wound; cloudy swelling of kidneys; peritonitis, generalized; amyloid degeneration, liver.

Bacteriology: Heart's blood: staphylococcus. Pericardium and pleural cavities sterile.

RESULTS AND DISCUSSION

The average stay per patient of the whole group of throat carriers admitted to the isolation wards from January to August was 22 days. These patients received only the routine treatment as described. The average period in isolation varied greatly from month to month; for instance, it was 28 days for those patients admitted in April; while for the month of May it was only 14 days. The treatment was the same for both months. Patients whose cultures were positive only once are not included in these averages. Some of these received the routine treatment while others were given none. In view of the great difference in the average length of stay in isolation from month to month and in view of the wide variation in stay of individual cases—6 days to 6 months—it seems that the form of treatment employed played little, if any, part in the removal of diphtheria bacilli from the individual throat. McCord and others[2] found that by standardizing their chlorcosane-dichloramine-T treatment, they reduced the average stay of convalescent carriers from 55 days in the first month of their report to 15 days in the last month; and the stay of contact carriers was reduced to 16 days for the last month of the report with an average of 23 days for 4 months. Our average for the whole time was 22 days; and for the last month it dropped to 14 days without any change in treatment. This may possibly have been influenced by the change in weather.

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[2] J. Am. Med. Assn., 1918, 71, p. 275.

Our experience with tonsillectomy, though limited, seems worth mentioning. Six patients who had been given routine treatment in isolation, for about a month, and who gave positive tonsillar crypt cultures, were selected. These cultures were made after swabbing the tonsils thoroughly with a 2% solution of dichloramine-T. to eliminate surface contamination. The periods in isolation for these patients before and after tonsillectomy were:

TABLE 1

PERIOD OF ISOLATION BEFORE AND AFTER TONSILLECTOMY

Patient	Period of Isolation Before Tonsillectomy, Days	Period of Isolation After Tonsillectomy, Days
G. C.	114	15
D. A.	37	10
D. S.	32	11
R. T.	31	6
J. W.	29	15
W. W.	51	21
Average	54	11.3

These patients received the same gargle-spray treatment before and after operation.

The tonsils from these patients were placed in 10% formaldehyde for 10 minutes, after which they were opened, and cultures were made from their centers. Diphtheria bacilli were obtained from all. It is believed that tonsillectomy is the operation of choice in certain cases. A few carriers who had had their tonsils removed previously were carrying bacilli in tags of tonsillar tissue and cleared up after a second operation.

The average stay in isolation of 14 wound carriers was 29.8 days. Here again the form of local application used seemed to be of little importance. The periods of isolation varied from 8 to 90 days, and there was a wide variation in the period for patients with the same types of wounds and under the same type of treatment. For instance, one patient who carried diphtheria bacilli in an amputation stump wound which became negative after 9 days in isolation, had been treated with alcohol dressings for the first two days, after which he had received nothing but dry sterile dressings. Another patient with the same type of wound, who received alcohol dressings, remained positive for 40 days. Six patients with infected amputation wounds of the thigh, were treated with dichloramine-T. and exposure to sunlight, twice daily. Their average isolation period was 15 days, which was much shorter than that for any other form of treatment, with the exception of the one case mentioned above. A number of cases were treated with dichloramine-T. alone without benefit. Careful cultural observations showed that the organisms were well below the surface of the wounds in practically all cases. In our experience the local applications mentioned above seemed to have little, if any, effect on the course of wound diphtheria carriers.

We had only 5 cases of active wound diphtheria and 2 of the patients died. In all of the cases, including the fatal ones, there was a marked decrease in the size of the membranes following the administration of diphtheria antitoxin. In one of the fatal cases, only 30,000 units of antitoxin were given, and the patient died of a diphtheria septicemia. Following the administration of 320,000 units of antitoxin in the other fatal case, about one-third of the membrane, which covered an area of 100 sq. cm. and extended over a large area of skin, loosened and came off. If the extent of the membrane is an indication of the degree of toxicity, extremely large doses of antitoxin are indicated in these cases. The immediate cause of death was probably peritonitis and septicemia, due to a staphylococcus infection, and not the diphtheria infection which was steadily improving. In the three patients that recovered, the membranes were not so extensive and disappeared promptly after the administration of from 20,000 to 30,000 units of antitoxin. In both of the fatal cases, the patients became extremely desiccated, and this factor was very troublesome. It appeared in both cases about 5 days before death, shortly after vomiting began. Intravenous administration of fluids was necessary as the emaciated condition of the patients did not permit a sufficient amount subcutaneously, and they were unable to retain any appreciable amount of fluids given by rectum. This desiccation, perhaps, could be prevented by giving a sufficiently large amount of antitoxin early in the course of the disease, but once present care should be taken to keep up a liberal fluid intake daily.

BACTERIOLOGIC

All primary cultures were made on Loeffler's serum and incubated at 37.5 C. for from 18 to 20 hours. Positive diagnoses were made only when Wesbrook's types A, B, C or D were found in stained preparations. Pure cultures were obtained by replating on horse whole blood agar, or serum agar. The diphtheria bacilli from 177 primary cultures all retained Gram's stain and showed polar granules when stained with methylene blue and by Neisser's method. No acid-fast organisms or granules were found.

VIRULENCE

Fifty-two strains, including 27 from contact throat carriers, 13 from convalescent throat carriers, 7 from wound carriers and 5 from wound cases, were tested to determine their virulence for guinea-pigs. Animals weighing 300 gm. were injected subcutaneously with 1.5 cc of a 72-hour broth culture, and in each instance control animals, inoculated intraperitoneally 24 hours previously with 100 units of diphtheria antitoxin, were given a similar dose. The percentage of virulent strains obtained from contact throat carriers and wound carriers were 48.1 and 42.8, respectively; while those from wound cases were 80% and from convalescent throat carriers 84.6%. Organisms of low virulence which killed guinea-pigs after 2 weeks, with typical local reactions, were not included in these percentages.

TABLE 2

VIRULENCE FOR GUINEA-PIGS

Source of Culture	Number Tested	Very Virulent		Low Virulence		Avirulent	
		Number	Per Cent.	Number	Per Cent.	Number	Per Cent.
Contact throat carriers	27	13	48.1	1	3,7	13	48.1
Wound carriers	7	3	42.8	1	14.2	3	42.8
Convalescent throat carriers	13	11	84.6	1	7.6	1	7.6
Wound cases	5	4	80.0	1	20.0	0	0.0
Total	52	31	59.6	4	7.6	17	32.6

CULTURAL CHARACTERISTICS

All cultures on Loeffler's serum were moist, confluent and grayish white. A few strains developed a yellowish tint after several days' incubation; none were proteolytic. The growth on whole blood-agar plates was moist, confluent, opaque and dark gray in color. A slight degree of hemolysis occurred with a few strains. The reactions with litmus milk were not striking; a small amount of acid was produced by three strains—no coagulation or clearing occurred. Pellicle formation with sedimentation was observed in all dextrose-broth cultures.

FERMENTATION OF CARBOHYDRATES

Tubes containing 1% each of C. P. glucose, saccharose, maltose, dextrin, inulin, mannite, lactose, xylose and arabinose, in 10 c.c. of sugar free infusion broth, were inoculated with standard amounts of pure cultures from each of 32 strains. The phenol red-china blue indicator of Morshima[3] was used, and the reaction of all mediums was made P_H. 7. Cultures were incubated at 37.5 C., and 4 readings were made at intervals of 2 days. Uninoculated tubes of each kind of carbohydrate broth were incubated as controls; and final readings were made by comparing the colors of the various cultures with a set of standard solutions. Twenty-three of the strains were virulent and 10 were avirulent; 17 were obtained from contact throat carriers, 8 from convalescent throat carriers, 2 from wound carriers and 6 from wound cases.

TABLE 3

FERMENTATION OF CARBOHYDRATES

Source of Cultures	Total	Virulence of Guinea-Pig	Glucose	Saccharose	Maltose	Dextrin	Inulin	Mannite	Lactose	Arabinose	Xylose
Contact throat carrier........	6	Very virulent	AC	ALK	AC	AC	ALK	ALK	*	NC	NC
Convalescent throat carrier...	5		AC	ALK	AC	AC	ALK	ALK		NC	NC
Wound case....................	3		AC	ALK	AC	AC	ALK	ALK		NC	NC
Wound carrier.................	1		AC	ALK	AC	AC	ALK	ALK		NC	NC
	—15										
Contact throat carrier........	4	Virulent	AC	ALK	AC	AC	ALK	ALK		NC	NC
Convalescent throat carrier...	3		AC	ALK	AC	AC	ALK	ALK		NC	NC
	— 7										
Contact throat carrier........	3	Avirulent	AC	ALK	AC	AC	ALK	ALK		NC	NC
Nose of fatal wound case......	1		AC	ALK	AC	AC	ALK	ALK		NC	NC
Wound carrier.................	1		AC	ALK	AC	AC	ALK	ALK		NC	NC
	— 5										
Contact throat carrier........	1	Avirulent	AC	NC	AC	NC	ALK	ALK	NC	NC	NC
	— 1										
Wound case....................	1	Virulent	AC	AC	ALK	ALK	ALK	ALK	ALK	NC	NC
	— 1										
Contact throat carrier........	3	Avirulent	AC	AC	ALK	ALK	ALK	ALK	ALK	NC	NC
Wound case....................	1		AC	AC	ALK	ALK	ALK	ALK	ALK	NC	NC
	— 4										

AC = acid, ALK = alkaline, and NC = no change.

* Reactions of lactose broth cultures were variable in first group; no change in 21, slightly acid in 4 and alkali in 2.

All of the 33 strains produced acid (P_H. 5.4-5.6) in glucose, and alkali (P_H. 7.3-7.6) in mannite and inulin; while no change occurred in the reaction of xylose or arabinose broth cultures. Saccharose cultures were made more alkaline (P_H 7.4-7.6) by 27 strains; acid was produced by one avirulent and one virulent wound case strain, and by 3 avirulent contact throat carrier strains; and no change in reaction occurred with one avirulent contact throat carrier strain. Maltose was fermented (P_H. 5.7-6) by all, except 1 avirulent and 1 virulent wound case, and 3 avirulent contact throat carrier strains. These 5 cultures showed an increase in alkali (P_H 7.3-7.6).

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[3] J. Infect. Dis., 1920, 26, p. 43.

Acid (P_H 6.4-6.7) was produced in dextrin broth by 27 cultures. There was no change in the reaction of one avirulent contact throat carrier culture; and alkali (P_H. 7.2-7.4) was produced in 3 avirulent contact throat carriers; one avirulent and one virulent wound case culture. Twenty-two strains produced no change in the reaction of lactose broth; 6 produced acid (P_H 6.5-6.6) and 7 produced alkali (P_H 7.4). As usual, the fermentation reactions gave no indication of the virulence of the organisms tested.

None of the strains produced indol in Dunham's peptone.

BLOOD CULTURES, ETC.

Blood cultures were made of 43 contact throat carriers, 9 convalescent throat carriers, 3 wound carriers and 2 wound cases; all were sterile with one exception. An atypical granular diphtheria-like bacillus was obtained in one flask of a blood culture from M., who was a contact throat carrier. This organism, however, differed culturally from diphtheriae and produced a fatal septicemia in guinea-pigs in spite of diphtheria antitoxin immunization. As a growth occurred in only one flask, this might have been a skin contamination. Urine cultures made from centrifugalized specimens of 26 carriers were all negative. Unclassified granular bacilli were obtained in 11 of them. No diphtheria bacilli were found in feces cultures of 21 carriers. A small amount of feces was broken up in glycerol and allowed to stand at room temperature for 48 hours, after which the precipitate was streaked on blood-agar plates and incubated.

The blood of 25 carriers was grouped for isohemo-agglutinins according to Jansky with the following results: group 1, 1 (4%); group 2, 6 (24%); group 3, (12%) and group 4, 15 or 60%. (Moss classification.)

Nasal cultures were positive on 30 of 44 contact throat carriers, 8 out of 9 active throat cases and 4 of 5 infected wound cases. Four of 5 wound cases had positive tonsillar surface cultures.

Tonsillar crypt cultures made from 44 contact throat carriers were positive in 24 instances, 7 of 9 active throat cases and 2 of 5 infected wound cases were positive.

Eight of 44 contact throat carriers and 1 of 5 wound cases had had their tonsils removed at some previous time. All of these were carrying bacilli in small tags of tonsillar tissue.

Complete blood counts and urine examinations made of all carriers failed to show any characteristic variation from the normal.

SUMMARY

Between October, 1918, and August, 1919, 75 cases of diphtheria and 102 carriers of diphtheria bacilli were treated at the Walter Reed General Hospital.

New cases continued to develop in the hospital each week, in spite of the isolation of all positive contacts until the summer months when the occurrence of diphtheria is generally lowest.

The successful treatment of carriers depended not so much on the kind of antiseptic used but on the ability to reach the organism with the antiseptic, or when possible on complete removal of the infected foci.

The danger of active wound infection should be recognized and early treatment with large doses of diphtheria antitoxin should be given.

Forty-eight and 42%, respectively, of the strains from contact throat carriers and wound carriers were very virulent, while 84.6% of those from convalescent throat carriers and 80% of those from wound cases were very virulent.

Neither morphology, fermentation reactions nor any other cultural characteristic gave any indication of the degree of virulence of the organisms studied.

No diphtheria bacilli were found in cultures of the blood, urine or feces of cases or carriers, except from one fatal wound case post-mortem.